This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (previously amended) An agent comprising:

a therapeutic component, and

a targeting ligand coupled to the therapeutic component, the targeting ligand being effective to bind to the alpha-2B or alpha-2B/alpha-2C adrenergic receptor subtype(s).

2. (original) An agent according to claim 1 wherein the therapeutic component interferes with the release of neurotransmitters from a cell or its processes.

3. (original) An agent according to claim 2 wherein the therapeutic component comprises a light chain component.

4. (previously amended) An agent according to claim 2 wherein the light chain component comprises a light chain or a fragment thereof of a botulinum toxin, a butyricum toxin, a tetani toxin or biologically active variants thereof.

5. (previously amended) An agent according to claim 2 wherein the light chain component comprises a light chain or a fragment thereof of a botulinum toxin type A, B, C1, D, E, F, G or biologically active variants thereof.

6. (previously amended) An agent according to claim 2 wherein the light chain component comprises a light chain or a

fragment thereof of a botulinum toxin type A or biologically active variants thereof.

7. (original) An agent according to claim 1 wherein the therapeutic component inactivates cellular ribosomes.

8. (original) An agent according to claim 7 wherein the therapeutic component is saporin.

9. (original) An agent according to claim 1 which further comprises a translocation component.

10. (currently amended) An agent according to claim 9 wherein the translocation component facilitates the transfer of at least a part of the agent into [[the]] a cytoplasm of the target cell.

11. (currently amended) An agent according to claim 9 wherein the translocation component facilitates the transfer of the therapeutic component into [[the]] a cytoplasm of the target cell.

12. (original) An agent according to claim 9 wherein the translocation component comprises a heavy chain component.

13. (previously amended) An agent according to claim 12 wherein the heavy chain component comprises a heavy chain or a fragment thereof of a botulinum toxin, a butyricum toxin, a tetani toxin or biologically active variants thereof.

14. (previously amended) An agent according to claim 12 wherein the heavy chain component comprises a heavy chain or a

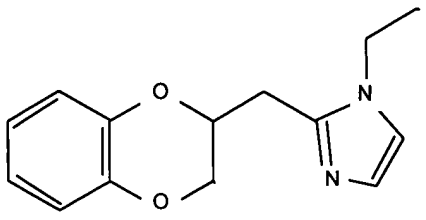
fragment thereof of a botulinum toxin type A, B, C1, D, E, F, G or biologically active variants thereof.

15. (previously amended) An agent according to claim 12 wherein the heavy chain component comprises a heavy chain or a fragment thereof of a botulinum toxin type A or biologically active variants thereof.

16. (currently amended) An agent according to claim 15 wherein the fragment of the heavy chain comprises at least a portion of [[the]] an amino terminal fragment of the heavy chain.

17. (currently amended) An agent according to claim [[1]] 9 wherein the therapeutic component comprises a light chain of a botulinum toxin type A and the translocation component comprises a fragment of a heavy chain of a botulinum toxin type A, wherein the fragment of a heavy chain can assist in the translocation of at least the therapeutic component into a cytoplasm of a cell.

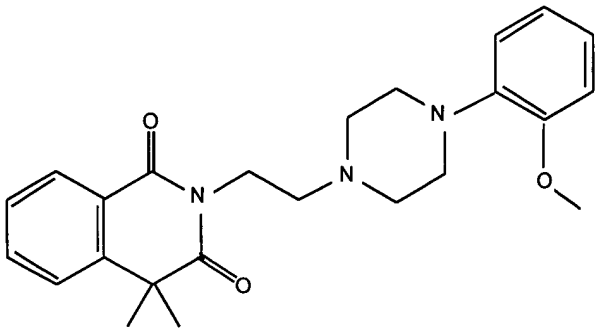
18. (currently amended) An agent according to claim 1 wherein the targeting ~~component~~ ligand is represented by the formula:



Imiloxan

[[I.]]

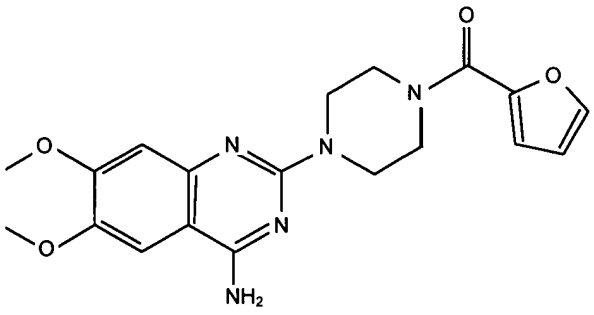
19. (currently amended) An agent according to claim 1 wherein the targeting ~~component~~ ligand is a compound represented by the formula:



~~ARC 239~~

[[II.]]

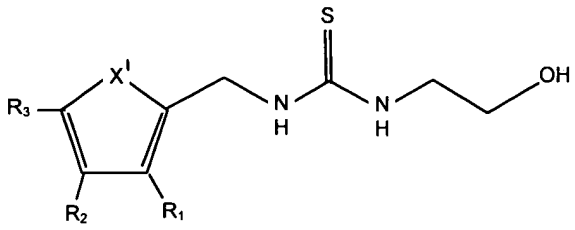
20. (currently amended) An agent according to claim 1 wherein the targeting ~~component~~ ligand is a compound represented by the formula



~~Prazosin~~

[[III.]]

21. (currently amended) An agent according to claim 1 wherein the targeting ~~component~~ ligand is a compound represented by the formula:



[[IV.]]

wherein X' is selected from the group consisting of R_4-C=C-R_5 and R_4-C;

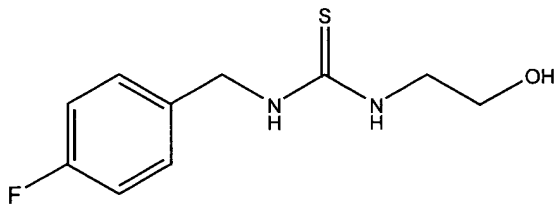
a six membered carbon ring structure is formed when X' is R_4-C=C-R_5;

a five membered carbon ring is formed when X' is R_4-C;

R_1, R_2, R_3, R_4 and R_5 are each independently selected from the group consisting of F, Cl, Br, I, OR_6 and H, wherein R_6 is H or an alkyl, including a methyl, an ethyl or a propyl.

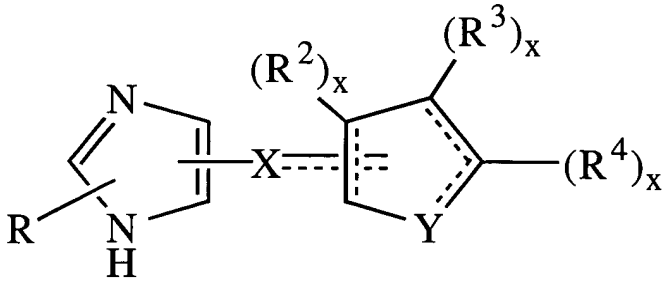
22. (canceled)

23. (currently amended) An agent according to claim 1 wherein the targeting ~~component~~ ligand is a compound represented by the formula:



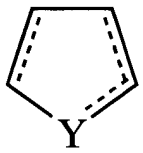
[[VI.]]

24. (currently amended) An agent according to claim 1 wherein the targeting ~~component~~ ligand is represented by the formula



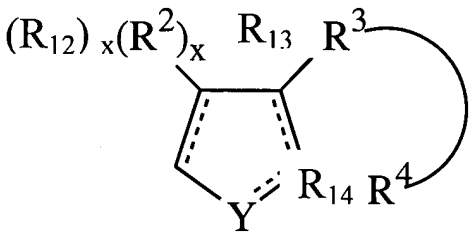
[[VII.]]

wherein the dotted lines represent optional double bonds; R is H or lower alkyl; X is S or $C(H)R_{11}$, wherein R_{11} is H or lower alkyl or R_{11} is absent when X is S or when the bond between X and the ring represented by



is a double bond; Y is O, N, S, $(C(R_{11})X)_y$, wherein y is an integer of from 1 to 3, -CH=CH- or $-Y_1CH_2-$, wherein Y_1 is O, N or S; x is an integer of 1 or 2, wherein x is 1 when R_{12}, R_{13} or R_{14} is bound to an unsaturated carbon atom and x is 2 when R_{12}, R_{13} or R_{14} is bonded to a saturated carbon atom; R_{12} is H, lower alkyl, halogen, hydroxy, lower alkoxy, lower alkenyl, acyl or lower alkynyl or, when attached to a saturated carbon atom, R_{12} may be oxo; R_{13} and R_{14} are, each, H, lower alkyl, halogen, lower alkenyl, acyl or lower alkynyl, or, when attached to a saturated carbon atom, R_{12} may be oxo; R_{13} and R_{14} are, each, H, lower alkyl, halogen, lower alkenyl, acyl, lower alkynyl, aryl, heteroaryl, or substituted aryl or heteroaryl, wherein said substituent is halogen, lower

alkyl, lower alkoxy, lower alkenyl, acyl, lower alkynyl, nitro, cyano, trifluoromethyl, hydroxy, or phenyl or, together, are -$(C(R_2)x)z$-; -$Y_1(C(R_2)x)z'$-; - Y_1 $(C(R_2)x)y$ Y_1-; -$(C(R_2)x)$- Y_1-$(C(R_2)x)$-; -$(C(R_2)x)$- Y_1-$(C(R_2)x)$-$(C(R_2)x)$- and - Y_1-$(C(R_2)x)$- Y_1-$(C(R_2)x)$- wherein z is an integer of from 3 to 5, z' is an integer of from 2 to 4 and x and y are as defined above, and further either end of each of these divalent moieties may attach at either R_{13} or R_{14} to form the condensed ring structure



and the ring thus formed may be totally unsaturated, partially unsaturated, or totally saturated provided that a ring carbon has no more than 4 valences, nitrogen no more than three and O and S have no more than two.

25. (currently amended) An agent according to claim 1 wherein the targeting ~~component~~ ligand comprises an amino acid component.

26. (original) An agent according to claim 25 wherein the amino acid component is an antibody.

27. (original) An agent according to claim 26 wherein the antibody is raised from an antigen component, the antigen component comprises a second extracellular loop of an alpha-2B receptor.

28. (original) An agent according to claim 27 wherein the second extracellular loop is conjugated to a keyhole limpet hemocyanin.

29. (canceled)

30. (original) An agent according to claim 25 wherein the amino acid component comprises a variant peptide, a variant polypeptide, a variant protein or a variant protein complex of a wild type peptide, polypeptide, protein or protein complex, respectively.

31. (original) An agent according to claim 25 wherein the amino acid component is a variant polypeptide.

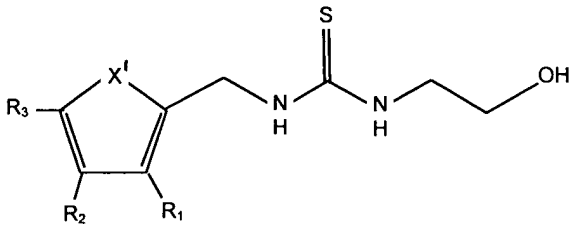
32. (original) An agent according to claim 31 wherein the variant polypeptide is a variant heavy chain.

33. (currently amended) An agent according to claim 1 wherein the therapeutic component and the targeting ~~component~~ ligand are attached to each other through a spacer component.

34. (currently amended) An agent according to claim 9 wherein the therapeutic component, the translocation component and the targeting ~~component~~ ligand are attached to each other through a spacer component.

35. (currently amended) An agent according to claim 34 wherein the therapeutic component is a light chain of a botulinum toxin type A, the translocation component is a fragment of a heavy chain of a botulinum toxin type A which can

facilitate the translocation of at least the light chain into a cytoplasm of a cell, and the targeting component is represented by the formula:



[[IV.]]

wherein X' is selected from the group consisting of R_4-C=C-R_5 and R_4-C;

a six membered carbon ring structure is formed when X' is R_4-C=C-R_5;

a five membered carbon ring is formed when X' is R_4-C;

R_1, R_2, R_3, R_4 and R_5 are each independently selected from the group consisting of F, Cl, Br, I, OR_6 and H, wherein R_6 is H or an alkyl, including a methyl, an ethyl or a propyl.

36. (original) An agent according to claim 34 wherein the spacer component comprises a moiety selected from the group consisting of a hydrocarbon, a polypeptide other than an immunoglobulin hinge region, and a proline-containing polypeptide identical or analogous to an immunoglobulin hinge region.

37. (original) An agent according to claim 1 useful for treating chronic pain in a mammal, including a human.

38. (original) An agent according to claim 37 wherein the chronic pain is treated without substantially affecting acute pain sensation or tactile sensation.

39. (previously amended) A method for making an agent for treating pain comprising the step of producing a polypeptide from a gene having codes for at least one component of the agent, wherein the agent comprises

a therapeutic component, and

a targeting ligand coupled to the therapeutic component, the targeting ligand being effective to bind to the alpha-2B or alpha-2B/alpha-2C adrenergic receptor subtype(s).

40. (original) A method for making an agent according to claim 39 wherein the agent further comprises a translocation component.

41. (currently amended) A method according to claim 40 wherein the therapeutic component comprises a light chain of botulium toxin type A and the translocation component comprises a fragment of a heavy chain which is able to facilitate the transfer of at least the light chain into [[the]] a cytoplasm of the target cell.

42. (currently amended) A method according to claim 40 wherein the targeting ~~component~~ ligand comprises an amino acid component.

43. (currently amended) A method according to claim 42 wherein the amino acid component comprises a variant peptide, a variant polypeptide, a variant protein, or a variant protein complex of a wild type peptide, polypeptide, protein or protein complex, respectively.

44. (original) A method according to claim 43 wherein the variant peptide is a variant heavy chain.

Claims 45-67 (canceled)

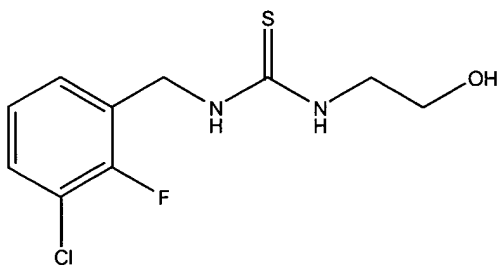
68. (previously added) The agent of claim 1, wherein the targeting ligand selectively binds to the alpha-2B or alpha-2B/alpha-2C adrenergic receptor subtype(s) as compared to the alpha-2A adrenergic receptor subtype.

69. (previously added) The method of claim 39, wherein the targeting ligand of the agent selectively binds to the alpha-2B or alpha-2B/alpha-2C adrenergic receptor subtype(s) as compared to the alpha-2A adrenergic receptor subtype.

70. (currently amended) An agent comprising:

a therapeutic component, and

a targeting component coupled to the therapeutic component, the targeting component being represented by the formula:



[[V.]]

71. (previously added) An agent comprising:

a therapeutic component, and

a targeting component coupled to the therapeutic component, the targeting component comprising an antibody raised from an antigen component comprising a second extracellular loop, the second extracellular loop comprising an amino acid sequence of KGDQGPQPRGRPQCKLNQE (SEQ ID NO: 1).